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(54) PROCESS AND APPARATUS FOR THE PRODUCTION OF STERILE WATER

(57) A process and an apparatus for the continuous production of pyrogen-free sterile water from untreated water in which the water is pressurised, pre-filtered, subjected to an ion-exchange process, and then is subjected to a reverse osmosis process in which the permeate comprises the pyrogen-free sterile water and the concentrate is returned to the untreated water prior to pressurisation. Provision is made for the removal of the heat generated during the pressurising step. Preferably the prefiltering is accomplished by a second reverse osmosis step. The pyrogen-free sterile water thus produced can be used in injection and infusion solutions and in eye medicaments.

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SPECIFICATION

PROCESS AND APPARATUS FOR THE PRODUCTION OF PYROGEN-FREE STERILE WATER

The invention relates to a process for the production of pyrogen-free sterile water, especially for injection and infusion solutions and eye medicaments, from drinking or other untreated water, and to an apparatus for carrying out this process.

The production of pyrogen-free sterile water by the conventional method of distillation requires multiple repetition of the distillation process, which is expensive in terms of apparatus and wasteful of energy. On the other hand the desired freedom from pyrogens, that is say the freedom of the obtained water from pathogenic substances, such as is required especially for the above-mentioned purposes, cannot be achieved by a single distillation.

Furthermore, it is known to produce sterile water by the use of ion exchangers and membrane-or depth-filters having such a fine pore size that germs and particles are separated by these filters. If the pore size of the filters is less than 0.22 μm, in this way a sterile liquid is produced. However germs have the property of settling onto such membranes, multiplying there and finally corroding the membranes, which is called "interpenetration of the germs". If only a single germ has penetrated through the membrane the entire system must be renewed. Furthermore, such membrane-or depth filters are also not capable of holding back pathogenic substances to a sufficient extent

It is the problem of the invention to provide a process and an apparatus for its execution which can deliver pyrogen-free sterile water avoiding multiple disillation which is expensive in terms of apparatus and wasteful of energy.

According to the invention this problem is solved according to the process in that the untreated water is brought to elevated pressure and after pre-filtration and ion exchange is subjected to reverse osmosis, the permeate of which can be withdrawn as sterile water, while the concentrate is added again to the untreated water before the pressure elevation.

The invention makes use of the property known *per se* of the diffusion effect in reverse osmosis, of holding back pyrogenic substances, and links this property with the preceding known separation of mineral substances in the ion exchange which is not adequately possible by the reverse osmosis, while with the return of the concentrate occurring in the reverse osmosis the germs and particles which occur in the ion exchange are immediately transported further and returned to the starting point of the process, where they are held back by the pre-filtration and thus separated out of the water circulating afresh.

With the increase of pressure of the untreated water naturally a certain increase of temperature is involved which due to the renewed introduction of the concentrate into the water circulation could lead to an undesired build-up of the temperature in the system. In order to avoid this according to a first development feature of the process according to the invention the heat occurring in the pressure increase of the untreated water is conducted away by increasing of the utilised quantity of untreated water and throttled draining of the excess untreated water after the pressure rise.

The pre-filtration of the untreated water before the ion exchange can *per se* take place in any desired manner. However it is especially expedient to effect the pre-filtration at least partially by a further reverse osmosis the permeate of which is subjected to the ion exchange, while concentrate then occurring is returned to the untreated water before the pressure rise. The removal of heat can here advantageously be effected in that a part of the concentrate of the reverse osmosis used for pre-filtration is conducted away as waste water.

An apparatus for carrying out the above-described process is characterised in accordance with the invention by the series-connection of a pump, a pre-filter, at least one ion exchange apparatus and a reverse osmosis apparatus, the concentrate exit of which is connected through a non-return valve with the pump entry, while the membrane of the reverse osmosis apparatus is selected so that it hinders pyrogenic substances from the diffusion taking place through it. A drain conduit conducted through a throttle expediently here branches off after the pump and a part of the water heated in the pump is constantly conducted away through this drain conduit, with corresponding increase of the untreated water supply.

In an advantageous development of the apparatus according to the invention the pre-filter is formed by a second reverse osmosis apparatus, the permeate exit of which is connected to the ion exchange apparatus and the concentrate exit of which is connected through a non-return valve with the pump entry. The above-mentioned removal of the heat generated in the pump is in this case expediently obtained in that the concentrate exit of the second reverse osmosis apparatus is connected through a throttle with a waste water outlet, and the connection conduit to the pump entry, likewise containing a throttle, branches off before this above-mentioned throttle.

In order to ensure an adequate througput of pyrogen-free sterile water through the first reverse osmosis apparatus, according to another feature for the advantageous development of the apparatus according to the invention, a throttle is arranged in the connection conduit between the concentrate exit of the first reverse osmosis apparatus and the pump entry.

It is obvious that the above-mentioned throttles determine the volumetric ratio of permeate to concentrate in the reverse osmosis apparatuses

and the volumetric ratio of waste water to returned concentrate. In order to optimise these ratios, a further development feature of the invention provides that at least some of the throttles are made adjustable.

It is obvious that the apparatus according to the invention is capable of continuously supplying pyrogen-free sterile water as permeate from the first-mentioned reverse osmosis apparatus. Unless this water is also constantly utilised, its storage raises special problems. In fact special storage vessels, for example of chemical-proof glass of hydrolitic Class 1 would have to be used for this purpose, for which moreover a sterile air supply and exhaustion would have to be provided. If on the other hand the apparatus were to be shut down, germs and organic substances would multiply accumulatively, which understandably must be prevented. Accordingly, in order that the apparatus may be operated continuously even without the special expense for storage vessels, a special development feature of the invention provides that the permeate exit of the first reverse osmosis apparatus is provided with a shut-off valve from which there branches a return conduit, with a non-return valve contained therein, to the pump entry. As long as the shut-off valve is closed the permeate of the first reverse osmosis apparatus returns by way of this conduit to the starting point of the process and runs afresh through the system, with a corresponding reduction in the required quantity of untreated water.

Yet a further development feature provides that the ion exchange apparatus is followed by one or more mechanical filters for the separation of the impurities or particles coming from the ion exchange apparatus, whereby the possibility is avoided of the highly delicate membrane of the first reverse osmosis apparatus being charged and stressed with these particles or in the long term mechanically destroyed.

According to the local conditions the pressure of the untreated water in the untreated water supply—usually the public drinking water mains—can vary greatly. Since on the other hand the excess water pressure in the concentrate chamber of the second reverse osmosis apparatus must not have too great a value, in view of the membrane of the apparatus, and accordinlgy the pump must not deliver too high a water pressure, there is the danger that in the case of too high a pressure in the untreated water supply an adequate return of the concentrate, under only a slight excess pressure, from the first reverse osmosis apparatus to the pump entry may not take place. In order to preclude this danger a pressure-reduction valve ensuring a limited untreated water pressure at the pump entry is expediently arranged in the untreated water supply. Another possibility for avoiding this danger consists of the arrangement of a pressureless sump from which the pump draws and into which both the untreated water conduit and the return conduits from the concentrate chambers open, at least the entry of the untreated water conduit taking place by way of an air gap.

The process according to the invention will be explained in greater detail below with reference to an apparatus for carrying out the invention which is represented by way of example in the accompanying drawing.

In the drawing 10 designates an untreated water supply by which drinking water or other untreated water is fed by way of a pressure-reduction valve 12, a mechanical pre-filter 14 and a non-return valve 16 to a pump 18 which brings the untreated water, which is kept in the pressure-reduction valve at a pressure for example of 1 bar, up to a pressure for example of 14 bars in the pump delivery conduit 20. The delivery conduit 20 of the pump 18 opens into the concentrate chamber 22 of a reverse osmosis apparatus 24 which contains a membrane 28 separating the concentrate chamber 22 from a permeate chamber 26.

From the concentrate chamber 22 of the reverse osmosis apparatus 24 a concentrate conduit 30 leads to a branching point 32 from which firstly a drainage conduit 34 with an adjustable throttle 36 contained therein branches. Moreover from the branching point 32 a return conduit 42 containing an adjustable throttle 38 and a non-return valve 40 leads to an entry point 44 in the untreated water supply, between the non-return valve 16 and the pump 18.

From the permeate chamber 26 of the reverse osmosis apparatus 24 a permeate conduit 46 leads by way of two series-connected ion exchange apparatuses 48, 50 and one or more mechanical filters 52 to the concentrate chamber 54 of a further reverse osmosis apparatus 56 which is provided with a membrane 58, preventing the diffusion of pyrogenic substances, for the separation of the concentrate chamber 54 from a permeate chamber 60. The use of two series-connected ion exchange apparatuses 48, 50 has the advantage that either one of these apparatuses can be regenerated without interrupting the ion exchange, which is essential after a specific working time.

From the concentrate chamber 54 of the reverse osmosis apparatus 56 a concentrate conduit 62 leads by way of an adjustable throttle 64 and a non-return valve 66 to the entry point 44 in the untreated water supply between the non-return valve 16 and the pump 18 therein. From the permeate chamber 60 of the reverse osmosis apparatus 56 a permeate conduit 68 leads by way of a shut-off valve 70 to the user. Before the shut-off valve 70 a conduit 74 containing a non-return valve 72 branches off and opens at 76 into the concentrate conduit 62 between the throttle 64 and the non-return valve 66.

The capacity of the reverse osmosis apparatus 24 is preferably substantially greater than, for example three times as great as, the capacity of the reverse osmosis apparatus 56.

Furthermore the throttles 36, 38, 64 are set so that the quantity of concentrate which departs

from the reverse osmosis apparatuses 24, 56 is substantially greater than, for example two to three times as great as, the issuing quantity of permeate. By way of example the following flow quantities occur in the individual conduits:— Let it be assumed that the shut-off valve 70 is opened for the withdrawal of pyrogenic sterile water fit for use from the permeate chamber 60 of the reverse osmosis apparatus 56 and the entire apparatus is designed so that the withdrawn quantity of water fit for use amounts here to 12 l/h (litres per hour). The quantiy of untreated water needed for this purpose, in view of the cooling of the pump, then amounts for example to quadruple, namely 48 l/h in the untreated water conduit 10, of which 36 l/h are drained away again through the drain conduit 34. The quantity of water passing through the pump 18 and the reverse osmosis apparatus 24 is however substantially greater as a result of the return of concentrate from the reverse osmosis apparatus 24 by way of the return conduit 42 and of concentrate from the reverse osmosis apparatus 56 by way of the return conduit 62 to the entry point 44 in the return water conduit 10, and amounts to 108 l/h, of which 72 l/h leave the concentrate chamber 22 of the reverse osmosis apparatus 24 by way of the concentrate conduit 30. Half of this quantity, namely 36 l/h, is returned through the return conduit 42 in the untreated water supply 10 again, while the remaining 36 l/h leave the system through the throttle 36 and the drain conduit 34. The remaining 36 l/h of the quantity of 108 l/h supplied to the reverse osmosis apparatus 24 diffuse through the membrane 28 of this apparatus and leave the permeate chamber 26 by way of the permeate conduit 46, flow through the ion exchange apparatuses 48, 50 and the mechanical filter 52 and pass to the concentrate chamber 54 of the reverse osmosis apparatus 56. Of these 36 l/h, 24 l/h of concentrate flow out of the concentrate chamber 54 of the reverse osmosis apparatus 56 through the conduit 62 with the throttle 64 and the non-return valve 66 back to the entry point 44 in the untreated water conduit 10, while the remaining 12 l/h diffuse through the membrane 58 of the reverse osmosis apparatus 56 and leave the apparatus through the permeate conduit 48 and the shut-off valve 70 as pyrogen-free sterile water fit for use.

The above flow rate figures show that the volumetric ratio between concentrate and permeate both in the reverse osmosis apparatus 24 and in the reverse osmosis apparatus 56 amounts to 3:1, which corresponds approximately to the optimum volumetric ratio of these apparatuses.

If the shut-off valve 70 is closed, nevertheless the throughput through the membrane 58 of the reverse osmosis apparatus 56 is maintained with a flow rate of 12 l/h, in that this quantity of water is capable of flowing back through the conduit 24 with the non-return valve 72 into the conduit 62 and thus the quantity of water re-entering the untreated water supply 10 through this conduit is increased to 36 l/h. Thus the required quantity of untreated water in the conduit 10 before the entry point 44 drops automatically to 36 l/h.

As can be seen, with the closure of the shut-off valve 70 nothing changes in the throughput of the reverse osmosis apparatuses. Rather the system continues to work uninterrupedly and the membranes 28, 58 of the reverse osmosis apparatuses are continuously further washed on the concentrate side, whereby the settlement of germs is largely prevented and thus destruction of the membranes is avoided.

In place of the reverse osmosis apparatus 24 a mechanical filter can also be used which then takes over the pre-filtration of the water supplied to the ion exchange apparatuses 48, 50. Then the concentrate conduit 30 is omitted and replaced by the conduit 78 entered in chain lines in the drawing, which branches off directly behind the pump 18 from its delivery conduit 20 and in part conducts away the excess water necessary for the cooling of the pump, by way of the drain conduit 34 and in part returns this excess through the throttle 38 and the non-return valve 40 in the return conduit 42 to the pump entry.

As can be seen, in the above-described example in the production of the pyrogen-free sterile water fit for use, as long as this water is withdrawn, only about three times the quantity of untreated water is lost, which can be tolerated in view of the simplicity in the assembly of the apparatus and the effective cooling of the pump nevertheless achieved therein. This loss of untreated water is justified, even in the case of an interruption of the withdrawal of water fit for use by closure of the shut-off valve 70, as a result of the water circulation through the two reverse osmosis apparatuses which is then maintained, thus preventing destruction of the membranes contained therein by multiplication of germs and other organic substances.

Finally the pump 18 can also draw from a pressureless sump which then replaces the entry point 44 and is fed both by the untreated water conduit 10 and by the concentrate chambers 22 and 44. As at least the entry of the untreated water conduit takes place by way of a free air gap, the pressure-reduction valve 12 and the non-return valve 16 can be omitted.

CLAIMS

1. A process for the production of pyrogen-free sterile water from untreated water comprising bringing the untreated water up to an elevated pressure and after pre-filtration and ion exchange, subjecting the water to reverse osmosis, the permeate of which comprises sterile water, while the concentrate is returned to the untreated water before the pressure elevation step.

2. A process as claimed in claim 1 wherein the heat occuring during the pressure rise of the untreated water is removed by increasing the utilised quality of untreated water and draining away with throttling of the excess untreated water after the pressure rise.

3. A process as claimed in either claim 1 or claim 2 wherein the pre-filtration step is at least partially effected by reverse osmosis, the permeate of which is subjected to ion exchange, while concentrate occuring therein is returned to the untreated water before its pressure rise.

4. A process as claimed in claim 3 wherein a part of the concentrate of the reverse osmosis used for the pre-filtration is drained away as waste water.

5. A process as claimed in claim 1 substantially as hereinbefore described with reference to the accompanying drawing.

6. An apparatus for carrying out a process as claimed in any one of the preceding claims comprising the series-series-connection of a pump, a pre-filter at least one ion exchange apparatus and a reverse osmosis apparatus the concentrate exit of which is connected through a non-return valve with the pump entry, the membrane of the reverse osmosis apparatus being selected so that it hinders the diffusion of pyrogenic substances through it.

7. An apparatus as claimed in claim 6 wherein a drain conduit conducted by way of a throttle branches off behind the pump so that a part of the water heated in the pump can be conducted away continuously, with an appropriate increase in the supply of untreated water, through this drain conduit.

8. An apparatus as claimed in either claim 6 or claim 7 wherein the pre-filter is formed by a second reverse osmosis apparatus, the permeate exit of which is connected to the ion exchange apparatus of apparatuses and the concentrate exit of which is connected through a non-return valve with the pump entry.

9. An apparatus as claimed in claim 8 wherein the concentrate exit of the second reverse osmosis apparatus is connected through a throttle with a waste water outlet, while before this throttle the connecting conduit to the pump entry likewise containing a throttle, branches off.

10. An apparatus as claimed in any one of claims 6 to 9 wherein a throttle is arranged in the connecting conduit between the concentrate chamber of the first reverse osmosis apparatus and the pump entry.

11. An apparatus as claimed in either claim 9 or claim 10 wherein at least some of the throttles are adjustable.

12. An apparatus as claimed in any one of claims 6 to 11 wherein the permeate exit of the first reverse osmosis apparatus is provided with a shut-off valve, before which a return conduit with a non-return valve contained therein branches off to the pump entry.

13. An apparatus as claimed in any one of claims 6 to 12 wherein the ion exchange apparatus or apparatuses are followed by one or more mechanical filters for the separation of impurities of particles occurring in the ion exchange apparatus or apparatuses.

14. An apparatus as claimed in any one of claims 6 to 13 wherein a pressure-reduction valve and a non-return valve are arranged in the untreated water supply conduit.

15. An apparatus as claimed in any one of claims 6 to 13 wherein the pump is preceded by a pressureless sump into which the untreated water supply conduit and the return conduits open, at least the entry of the untreated water conduit taking place by way of an air gap.

16. An apparatus as claimed in claim 6 substantially as hereinbefore described with reference to the accompanying drawing.

17. Pyrogen-free water when produced by a method or using an apparatus as claimed in any one of the preceding claims.

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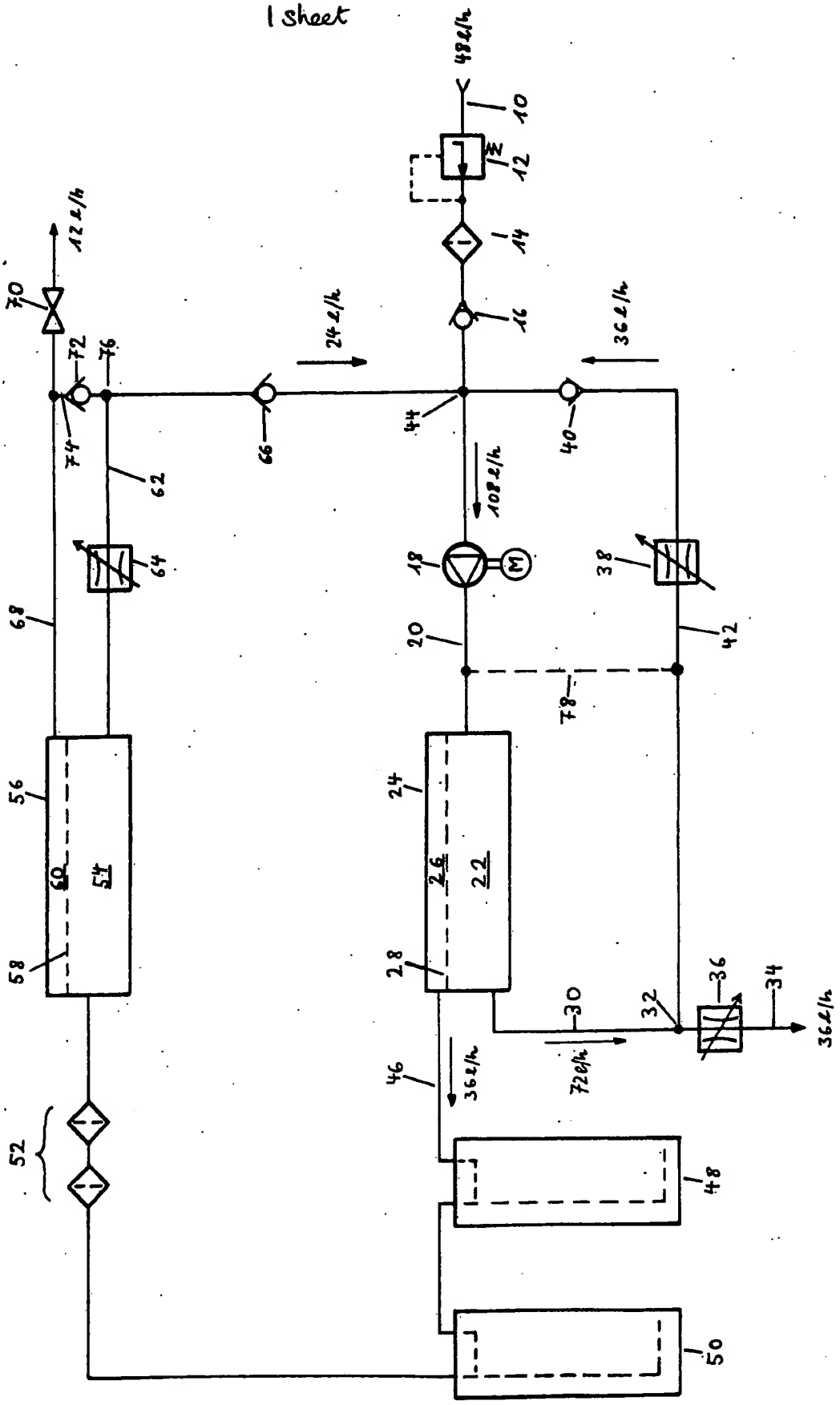
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